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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
400 TECHNOLOGY SQUARE
CAMBRIDGE, MA 02139

EXAMINER	
MACFARLANE, STACEY NEE	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,977	IOURGENKO ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *3,4,7,9,10,13,14,17 and 19-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5, 6, 8, 11, 12, 15, 16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group 2 and the specific species of "Huntington's disease" and the protein "CREAP 1" in the reply filed on April 4, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 3, 4, 7, 9, 10, 13, 14, 17, and 19-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions/ species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 4, 2008.

3. Claims 1, 2, 5, 6, 8, 11, 12, 15, 16 and 18, in so far as they read upon the elected species, will be examined upon their merits in the instant Office Action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2, 5, 6, 8, 11, 12, 15, 16 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 1, 6, 8, 11, 16 and 18 are vague and indefinite in so far as they employ the term "CREAP" as a limitation. This term is appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one

cannot determine the metes and bounds of "CREAP". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "CREAP" protein, an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

7. The term "inhibit(s)" in claims 6, 8, and 18 is a relative term which renders the claim indefinite. The term "inhibit" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

8. Claims 2, 5, 12 and 15 are indefinite for depending from indefinite claims.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 2, 5, 6, 8, 11, 12, 15, 16, and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claim 1 recites a method comprising administration of a CREAP modulator. Claims 2, 5, 6, 8, 11, 12, 15, 16, and 18 are dependent from Claim 1 and do not further limit the "CREAP modulator", and are therefore included in the rejection. The claims do

not require that the "modulator" possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of molecules that is identified only as being "modulators" and defined by the function of inhibiting the activity of any CREAP protein, and the instant specification fails to describe the entire genus of molecules that are encompassed by these claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant discloses a generalized description of CREAP modulators ("antisense oligonucleotides, triple helix DNA, ribozymes, RNA aptamers, siRNA and double or single stranded RNA ...antibodies to a CREAP protein or fragments thereof ... peptide mimetics of a CREAP protein," Specification page 3, last paragraph) but no specific examples of a modulator are given. The claims, however, encompass method of administration of any CREAP modulator that can inhibit the activity of any CREAP protein, thus, the claims are not limited to specific molecules with known structure. The specification delineates screening methods by which said modulators can be determined it does not actually identify a specific compound that has been shown to inhibit an activity of a CREAP protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics,

structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is a recitation of activity. There is not even the identification of any particular portion of a structure that must be conserved for CREAP modulatory activity. As stated above, it is not even clear what molecules are considered modulators. The specification does not provide a complete structure of either or those agonists and fails to provide a representative number of species for the recited genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the structure of the encompassed genus of modulators, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires more than a mere recitation of activity as part of the invention and a reference to a potential method of isolating or screening molecules that fulfill that activity requirement. The compound itself is required. See *Fiers v Revel*,

25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

11. Claims 1, 2, 5, 6, 8, 11, 12, 15, 16, and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

12. Claims 1, 2, 5, 6, 8, 11, 12, 15, 16, and 18 are drawn to a method to prevent, treat or ameliorate pathological conditions, namely neurodegenerative diseases and specifically Huntington's disease, comprising administering to a subject modulator that inhibits the activity of CREAP, and CREAP 1 protein in particular.

13. The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

14. Claims 1 and 11 broadly encompass methods for preventing, treating, or ameliorating pathological conditions related to abnormal activation of CRE-dependent gene expression or abnormal activation of chemokines comprising administering any CREAP modulator. In their broadest reasonable interpretation the methods encompass prevention and/or treatment of CRE-related genetic disorders, such as neurofibromatosis, chemokine-related genetic disorders, such has familial Rheumatoid arthritis, or the genetically inherited and instantly-elected Huntington's disease, by the administration of any molecule that modulates (increases or decreases) CREAP protein activity.

15. The invention is based solely on the identification of several isoforms of CREAP proteins and the finding that they activate CREB. The nature of the invention relates to methods of preventing, treating or ameliorating pathological conditions comprising administration of a CREAP modulator. The instant specification, however, provides no specific example of said modulator (see also section 10 above) and provides neither guidance, nor working examples that would show that the claimed method for in vivo prevention, treatment or amelioration of disease could be successfully achieved by administration of any CREAP modulator. Absent such guidance, one of ordinary skill in the art would require undue experimentation to discover how to practice Applicant's invention, as currently claimed.

16. The state of the art at the time of filing recognized a novel family of CRE-associated proteins (CREAPs) and CREAP 1 in particular (Ohara et al., NCBI accession number BAA31591, submitted May 1998) . As of the current date, however, there is no evidence of record of a nexus between CREAP protein activity and the etiology, pathology or symptomology of any disease.

17. With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the scope of enablement, the claims are analyzed with respect to the teachings of the specification and are to be given their broadest reasonable interpretation that is consistent with the specification. See MPEP 2111 [R-1], which states: "During patent examination, the pending claims must be "given [their] broadest reasonable interpretation consistent with the specification." In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969)".

18. As such, the broadest reasonable interpretation of the claimed method is that it allows for the treatment of a patient suffering from any pathological condition related to abnormal activation of CRE-dependent gene expression or abnormal activation of chemokines, comprising administering any agent that modulates CREAP. Thus, the claims encompass an unreasonable number of etiologically and pathologically distinct

conditions and disorders, as stated above, none which have a nexus or association with the CREAP activity. Thus, a skilled artisan would not know how to prevent or treat these diseases by mere administration of any CREAP modulator.

19. Furthermore, Claims 1 and 11 broadly encompass methods of prevention or treatment by administration of any CREAP modulator. MPEP 2164.08(a) defines a single means claim as a claim which covered every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the inventor. This type of claim was held to be nonenabling for the scope of the claim in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property (i.e. modulation up or down), a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure or means for achieving the stated result while the specification discloses at most only those known to the inventor. However as stated in section 10 above the inventor has not disclosed any specific example of a CREAP modulator but rather discloses a broad range of potential molecules. Thus, in the instant case the claims are not commensurate in scope with the specification. Applicant should note that the claims are so broad as to encompass any agent that kills the animal since the claims merely require that the modulator inhibit the activity of the CREAP protein and toxins or poisons that kill the animal are examples of inhibition taken to the extreme.

20. As opposed to what is claimed, what is disclosed about the claimed method is narrow: There are no working examples provided for in vitro inhibition of CREAP protein

activity by a specific modulator, nor an in vitro assay that would be predictive of in vivo results pertaining to prevention or treatment of disease. Furthermore, the disclosure provides general guidance as to the modulators that may be screened for use in the method but have not demonstrated the method as successfully achieved. As the following reference indicates, even currently within the art, much unpredictability remains with respect to the prevention of the neurodegenerative disease of Claim 2 and specifically the instantly-elected Huntington's disease of Claim 5 (Hersch and Rosas, Neurotherapeutics, 5:226-236, April 2008). Since the current art teaches that unpredictability remains and that Huntington's disease cannot be prevented, one of ordinary skill in the art would have to rely on the guidance within the instant specification in order to practice the method of prevention as claimed. The instant disclosure, however, has provided no guidance to indicate the practice of the method comprising the administration of any CREAP modulator with a reasonable expectation of success. Therefore, the disclosure provides no guidance as to how to use the claimed method.

21. The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 1001, (CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting

material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

22. Examiner concludes that the instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution. In the instant case, one of ordinary skill in the art would have to first correlate CREAP protein activity with disease pathology, develop modulators that inhibit the activity of the protein, successfully deliver them in vivo and demonstrate effective prevention or treatment of disease in order to practice the method as claimed. Such experimentation is not routine but constitutes undue experimentation in order to close the gaps between genetic, laboratory, and clinical data.

Conclusion

23. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M,W and ALT F 7 am to 3:30, T & R 5:30 -5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649